



PATENT SPECIFICATION

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PROVISIONAL SPECIFICATION

Improvements relating to the manufacture of the 1:4-3:6-Dianhydrides of Mannitol and Sorbitol

We, WALTER NORMAN HAWORTH, F.R.S., and LESLIE FREDERICK WIGGINS, both British Subjects, both of the University, Department of Chemistry, Edgbaston, in the City of Birmingham 15, do hereby declare the nature of this invention to be as follows:—

This invention has for its object to enable the 1:4-3:6-dianhydrides of mannitol and sorbitol to be produced from sucrose.

It is known that sucrose or invert sugar can be reduced to a mixture of mannitol and sorbitol by catalytic hydrogenation, or, in the case of invert sugar, by electrolytic reduction. It is also known that mannitol and sorbitol readily undergo loss of two molecules of water to give 1:4-3:6-dianhydro mannitol and 1:4-3:6-dianhydro sorbitol respectively. By our invention we are able to obtain these compounds in a pure crystalline state from sucrose.

According to our invention sucrose, or invert sugar obtained by acid hydrolysis of sucrose, is hydrogenated in a weakly alkaline buffered solution with a nickel catalyst to give a mixture of hexitols, that is to say a mixture of mannitol and sorbitol. The mixture of the two hexitols is then treated with an acid, which may be an inorganic acid, e.g., hydrochloric, sulphuric or phosphoric acid; or an organic acid, e.g., benzene sulphonic acid, *p*-toluene sulphonic acid. The mixture of dianhydro mannitol and dianhydro sorbitol thus obtained is then fractionally distilled, and the fractions are recrystallised giving pure 1:4-3:6-dianhydro mannitol and pure 1:4-3:6-dianhydro sorbitol. Alternatively a mixture of the two hexitols may be obtained by distillation without fractionation.

Example

0.1 N sulphuric acid (1900 parts) was brought to the boil and maintained in ebullition while sucrose (500 parts) was slowly added with stirring. When all the sucrose had been added the solution was maintained in ebullition for one minute, cooled and neutralised with barium hydroxide hydrate (32 parts). The barium sulphate was filtered (or centrifuged) off, and the filtrate was hydrogenated with 8.10 parts Raney nickel catalyst at 110–120°C. under 75–100 atmospheres of hydrogen for 6½ hours in the presence of sodium carbonate anhydrous (2 parts) and calcium carbonate (80 parts). The resulting mixture was filtered and the filtrate evaporated.

The mixture of hexitols was then refluxed for three days with concentrated hydrochloric acid (2310 parts). The resulting solution was evaporated under reduced pressure and the residue distilled at 12 mm. The distillate (230 parts) collected between 125–225°C. (bath temperature) consisted of the mixture of 1:4-3:6-dianhydro mannitol and 1:4-3:6-dianhydro sorbitol. This mixture was fractionally distilled and the fractions which solidified were recrystallised from ethyl acetate yielding dianhydro mannitol (34 parts), m.p. 85–87°C., b.p. 138°C./10 mm, and dianhydro sorbitol (143.0 parts), m.p. 57–61°C., b.p. 163°C./10 mm. The fraction between these two was a syrup (52.5 parts), b.p. 145–160°C./10 mm, which did not crystallise.

DATED this 18th day of September, 1945.

MARKS & CLERK.

COMPLETE SPECIFICATION

Improvements relating to the manufacture of the 1:4-3:6-Dianhydrides of Mannitol and Sorbitol

We, WALTER NORMAN HAWORTH, F.R.S., and LESLIE FREDERICK WIGGINS, both British Subjects, both of the University, Department of Chemistry, Edgbaston, in the City of Birmingham 15, do hereby declare the nature of this invention and in what

manner the same is to be performed, to be particularly described and ascertained in and by the following statement:—

This invention has for its object to enable the 1:4-3:6-dianhydrides of mannitol and sorbitol to be produced from sucrose.

It is known that sucrose or invert sugar can be reduced to a mixture of mannitol and sorbitol by catalytic hydrogenation, or, in the case of invert sugar, by electrolytic reduction. It is also known that mannitol and sorbitol readily undergo loss of two molecules of water to give 1:4-3:6-dianhydro mannitol and 1:4-3:6-dianhydro sorbitol respectively.

According to our invention sucrose, or invert sugar obtained by acid hydrolysis of sucrose, is hydrogenated (in an atmosphere of hydrogen at a pressure of 75-100 atmospheres and at a temperature of 110-120°C.) with a Raney nickel catalyst in the presence of sodium and calcium carbonates to give a mixture of hexitols, that is to say a mixture of mannitol and sorbitol. The mixture of the two hexitols is then treated with an acid, which may be an inorganic acid, e.g. hydrochloric, sulphuric or phosphoric acid; or an organic acid, e.g. benzene sulphonic acid, *p*-toluene sulphonic acid. The mixture of dianhydro mannitol and dianhydro sorbitol thus obtained is then fractionally distilled, and the fractions are recrystallised giving pure 1:4-3:6-dianhydro mannitol and pure 1:4-3:6-dianhydro sorbitol. Alternatively a mixture of the two dianhydro hexitols may be obtained by distillation with or without fractionation. A second alternative consists in removing the mannitol constituent of the mannitol-sorbitol mixture and converting only the residual sorbitol to 1:4-3:6-dianhydro sorbitol.

Example 1

0.1 N sulphuric acid (1900 parts by weight) was brought to the boil and maintained in ebullition while sucrose (500 parts by weight) was slowly added with stirring. When all the sucrose had been added the solution was maintained in ebullition for one minute, cooled and neutralised with barium hydroxide hydrate (32 parts by weight). The barium sulphate was filtered (or centrifuged) off, and the filtrate was hydrogenated with 8-10 parts (by weight) Raney nickel catalyst at 110-120°C. under 75-100 atmospheres of hydrogen for 6½ hours in the presence of sodium carbonate anhydrous (2 parts by weight) and calcium carbonate (80 parts by weight). The resulting mixture was filtered and the filtrate evaporated to give the mannitol-sorbitol mixture.

The mixture of hexitols was then refluxed for three days with concentrated hydrochloric acid (2310 parts by weight). The resulting solution was evaporated under reduced pressure and the residue distilled at 12 mm. The distillate (230 parts by weight) collected between 125-225°C. (bath temperature) consisted of the mixture of 1:4-3:6-dianhydro mannitol and 1:4-3:6-dianhydro sorbitol. This mixture was fractionally

distilled and the fractions which solidified were recrystallised from ethyl acetate yielding dianhydro mannitol (34 parts by weight), m.p. 85-87°C., b.p. 138°C./10 mm, and dianhydro sorbitol (143.0 parts by weight), m.p. 57-61°C., b.p. 163°C./10 mm. The fraction between these two was a syrup (52.5 parts by weight), b.p. 145-160°C./10 mm, which did not crystallise.

Example 2

The mixture of mannitol and sorbitol obtained from sucrose as in Example 1 was heated with concentrated sulphuric acid (5% of the weight of the hexitol mixture) and xylene (5 times the volume of the hexitol mixture) under distillation conditions for 2 hours with vigorous stirring so that the water formed during the reaction was azeotropically removed. The xylene was then decanted off, the residue dissolved in aqueous alcohol and the acid neutralized with sodium carbonate. The solution was filtered and evaporated under reduced pressure. The dianhydro hexitol mixture was then fractionally distilled as in Example 1.

Example 3

The mixture of mannitol and sorbitol obtained from sucrose as in Example 1 was heated with xylene (5 times the volume of the hexitol mixture) containing *p*-toluene sulphonic acid (5% of the weight of hexitols) under distillation conditions with vigorous stirring, so that water formed during the reaction was continuously removed. Thereafter the xylene was decanted off and the residue dissolved in aqueous alcohol and the acid neutralized with sodium carbonate. The solution was filtered and evaporated to dryness under diminished pressure and the residue fractionally distilled to give pure dianhydro mannitol and pure dianhydro sorbitol as described in Example 1.

Example 4

The mixture of mannitol and sorbitol obtained from sucrose as in Example 1 was dissolved in aqueous alcohol and the mannitol removed by crystallisation. The mother liquor, containing the sorbitol together with a small amount of residual mannitol was heated with concentrated sulphuric acid (5% of the weight of the hexitol) in xylene (5 times the volume of the hexitol taken) with vigorous stirring under distillation conditions for about 2 hours so that the water formed in the reaction was removed azeotropically. The xylene was then decanted off, the residue dissolved in aqueous alcohol, and the acid neutralized with sodium carbonate. The solution was then filtered and evaporated to dryness. The residue on distillation gave dianhydro sorbitol in high yield.

Having now particularly described and ascertained the nature of our said invention

and in what manner the same is to be performed, we declare that what we claim is:—

1. The manufacture of the 1:4-3:6-dianhydrides of mannitol and sorbitol from sucrose; or invert sugar, by hydrogenating the same (in an atmosphere of hydrogen at a pressure of 75-100 atmospheres and at a temperature of 110-120°C.) with a Raney nickel catalyst in the presence of sodium and calcium carbonates, to give a mixture of mannitol and sorbitol, and treating the said mixture with an appropriate acid to give a mixture of dianhydro mannitol and dianhydro sorbitol.
2. The manufacture of 1:4-3:6-dianhydrides of mannitol and sorbitol by the method claimed in Claim 1, and finally distilling (with or without fractionation) the mixture of dianhydro mannitol and dianhydro sorbitol.
3. A modification of the method claimed in Claim 1, which consists in removing the mannitol constituent of the mannitol-sorbitol

mixture and converting only the residual sorbitol to 1:4-3:6-dianhydro sorbitol.

4. The manufacture of 1:4-3:6-dianhydrides of mannitol and sorbitol, by the method claimed in Claim 1, in which the acid used is hydrochloric, sulphuric, or phosphoric acid.

5. The manufacture of 1:4-3:6-dianhydrides of mannitol and sorbitol by the method claimed in Claim 1, in which the acid used is benzene sulphonic, or p-toluene sulphonic, acid.

6. The manufacture of 1:4-3:6-dianhydrides of mannitol and sorbitol or of sorbitol alone as claimed in Claims 1 or 3, and in accordance with any of the above described examples 1-4.

7. 1:4-3:6-dianhydrides of mannitol and sorbitol when produced by the method claimed in any of the preceding claims.

DATED this 11th day of September, 1946.

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